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PULMONARY EFFECTS OF MULTILEVEL HeO_2 DIVES USING THE MK 16 MOD 1 UBA

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19. ABSTRACT: Flow-volume parameters were measured before and after a series of HeO_2 decompression dives that had been approved by the Institutional Review Board at Navy Experimental Diving Unit (NEDU). Divers also were asked about inspiratory burning, cough, shortness of breath, chest tightness, and rapid, shallow breathing. The dives were conducted in the Ocean Simulation Facility at NEDU, and had total dive times with PO_2 = 1.3 atm between 6.5 and 7 hours. Data were obtained from 89 dives using four different dive profiles and 55 divers. Details are provided by profile. In aggregate, on the day of diving, 25% of the divers reported respiratory symptoms, and 19% showed decreases in one or more indices of pulmonary function: forced vital capacity (FVC), forced expired volume in one second (FEV_1), forced expired flow between 25% and 75% of volume expired ($FEF_{25–75}$),and peak forced expired flow (FEF_{max}). On the day following the dive, 9.6% of subjects reported respiratory symptoms,19% showed decreases in one or more of those indices, and 8.2% reported exercise intolerance. These values are consistent with those from other studies of similar duration and PO_2 but with N_2O_2 or O_2 as breathing gas, studies in which 30% to 50% of subjects had experienced symptoms and 20% to 30% had deficits in pulmonary function immediately after diving.

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INTRODUCTION

To minimize pulmonary oxygen toxicity, the *U.S. Navy Diving Manual* limits dive time on the MK 16 MOD 1 to four hours per day and 16 hours per week.[1] (With the MK 16 MOD 1, oxygen partial pressure [P_{O_2}] is controlled to 1.3 atmospheres [atm] when the rig is deeper than 33 feet of sea water [fsw].) Oxygen time with 100% oxygen from the MK 25 similarly is restricted to four hours per day at most, and mixed gas diving with $P_{O_2} \geq 1$ atm is included in the oxygen time.[1]

Dives with oxygen times longer than four hours have been considered for specific purposes. During tests of decompression tables for several scenarios involving extended oxygen times,[2] we were able to measure pulmonary function before and after diving, to assess the incidence and severity of pulmonary oxygen toxicity from the exposures. We measured changes in pulmonary function and assessed symptoms both immediately after diving exposures and for at least one day following. Pulmonary function variables determined from forced flow-volume loops were forced vital capacity (FVC), forced expired volume in one second (FEV_1), peak expired flow or maximum forced expired flow (FEF_{max}), and average forced expiratory flow from 25% to 75% of expired volume ($FEF_{25–75}$). The lower limits of normal for pulmonary function variables were defined as the lower 95% confidence bands for each variable — that is, as baseline decreases relative to baseline of 2.4 times the coefficient of variation (cv) found for the Navy Experimental Diving Unit (NEDU) population: namely, 7.7% for FVC, 8.4% for FEV_1, 16.8% for FEF_{max}, and 17.0% for $FEF_{25–75}$.[3]

METHODS

GENERAL

During the dives in NEDU's Ocean Simulation Facility (OSF), divers were immersed in 80 ± 2 °F water for much of the dive time, then moved from the water to sit in warm chamber air. Chamber pressure was varied to simulate four different dive profiles. For the first part of each dive and at varying depths, submerged divers breathed from the MK 16 MOD 1 (P_{O_2} = 1.3 atm) with He as the inert gas in the diluent mixture. During decompression, divers sat with only their lower bodies in the water and continued to breathe from the MK 16 MOD 1. At the 20 fsw decompression stop, though, after a 15-minute period on chamber air as they moved to a dry chamber, divers breathed oxygen from the MK 25, with 15-minute air breaks after every hour. Divers rested throughout the dives except for a 45- to 60-minute exercise period at the greatest depth, where they alternated submerged weight lifting and treadmill walking. Details are given in the protocol, which was approved by NEDU's Institutional Review Board.[2]

Sixty-six individual divers enrolled in the study, and 55 participated, with up to three dives per person. The numbers diving each profile were 16, 26, 22, and 25. Divers were from NEDU and several other commands. All gave written informed consent.

For each diver, flow-volume parameters of pulmonary function were measured at a baseline session during the week before the individual's first dive, within an hour after surfacing from the dive, and usually on the day following the diving. As described in "PROCEDURES," some divers returned for further measurements, and some failed to return when they should have.

EXPERIMENTAL DESIGN AND ANALYSIS

Pulmonary function variables were considered to be different from baseline if they were outside the 95% confidence bands based on normal variability.[3] Confidence with α = 0.05 (95% confidence in the proportion) in estimates of the incidence of (1) changes in pulmonary function or (2) symptoms was obtained from the binomial distribution. Fisher's Exact Test was used to compute the probabilities that pairs of proportions represented samples from the same population.[4]

EQUIPMENT AND INSTRUMENTATION

The Collins CPL (Ferraris Respiratory; Louisville, CO) was used to record forced flow-volume loops to obtain measures of pulmonary function.

PROCEDURES

All oxygen time was nominally at P_{O_2} = 1.3 atm, and all four profiles included a total of 45 minutes of breathing chamber air at 20 fsw. Profile A1 provided 43 minutes of exercise time at a depth of 200 fsw and 6 hours and 56 minutes of oxygen time. Profile A2 involved 60 minutes of exercise at 200 fsw and 6 hours and 33 minutes of oxygen time. Profile A3 included 49 minutes of exercise at 180 fsw and 6 hours and 42 minutes of oxygen time. Profile A4 had 56 minutes of exercise at 160 fsw and 6 hours and 56 minutes of oxygen time.[2]

To measure pulmonary function, at each session we acquired three flow-volume loops that were performed and repeatable by American Thoracic Society standards.[5] FVC, FEV_1, FEF_{max}, and $FEF_{25–75}$ were read from these flow-volume loops. We did not measure diffusing capacity of the lung.

Baseline pulmonary function was tested within the week before the test dives. The averages of three properly performed flow-volume loops were used for comparisons with later values. Flow-volume curves were measured within an hour of surfacing and one day after each dive. If FVC, FEV_1, FEF_{max}, or $FEF_{25–75}$ was below the lower limit of normal variability around baseline, the measurement was repeated on following days until pulmonary function was within those limits or the diver was lost to follow-up. (Unfortunately, most divers who had travelled to participate in this study were lost to follow-up because they returned home; some also neglected to return even on the day after diving.) Any value below normal limits was considered to indicate an incident of altered pulmonary function.

At each session when pulmonary function was measured, divers were questioned about respiratory symptoms, visual complaints, ear discomfort, and unusual fatigue or exercise intolerance. Specific respiratory symptoms queried were chest tightness, shortness of breath, rapid shallow breathing, and cough. After the dives, the divers were also asked to report any symptoms they remembered from their air breaks during decompression.

Incidences of symptoms and of changes in pulmonary function were calculated as the number of divers with one or more symptoms or changes in pulmonary function, divided by the total number of divers completing the profile.

RESULTS

INCIDENCES OF SYMPTOMS AND SIGNS

Details of respiratory symptoms, pulmonary function changes, and any exercise intolerance or fatigue reported for the four profiles are shown in Tables 1–4. Fatigue and exercise tolerance, combined as one symptom in these tables, was not included in the incidence of respiratory symptoms.

<u>Profile A1</u>

Seven of 16 subjects reported mild respiratory symptoms during the dive or immediately after surfacing. Although most symptoms were mild, for one subject they were multiple and moderate, and three other subjects experienced multiple mild symptoms. Of the 15 subjects available on the day after diving (Day+1), four subjects, two of whom reported symptoms only that day, presented respiratory symptoms. One subject with symptoms both after diving and on Day+1 had reported symptoms of an upper respiratory infection (URI) even before the dive, but the multiple symptoms, several of which are not usual for a URI, are considered to represent pulmonary oxygen toxicity.

Four subjects showed reduced indices of pulmonary function immediately after diving, and three of those had lingering changes on Day+1, when another diver showed changes for the first time. Three subjects reported symptoms and also showed decreases in indices of pulmonary function that lasted two days, while two subjects showed depressed flow-volume parameters but did not report symptoms. Two subjects reported fatigue or exercise intolerance on Day+1.

After Profile A1 (43 minutes of exercise time; 6 hours and 56 minutes of oxygen time), the incidence of respiratory symptoms on the dive day was 43.8%, and the binomial confidence interval (CI) was 19.7% to 70.2%. On Day+1 the incidence of respiratory symptoms was 26.7%, and the binomial CI was 7.7% to 55.1%. The incidence of any decrease in a flow-volume parameter on the dive day was 25.0%, and the binomial CI was 7.2% to 54.4%. On Day+1 the incidence of flow-volume changes was 26.7%, and the binomial CI was 7.7% to 55.1%.

Table 1.
Decreases in pulmonary function and symptoms of pulmonary oxygen toxicity after Profile A1

Diver	During or immediately after dive	Day+1
11a	i $FEF_{25–75}$, –22%	f FEV_1, –8.9% $FEF_{25–75}$, –26%
11c	i FEV_1, –17.2% $FEF_{25–75}$, –40%	r FVC, –8.5% FEV_1, –18.2% $FEF_{25–75}$, –40%
18	c $FEF_{25–75}$, –22%	— FEV_1, –9.8% $FEF_{25–75}$, –27%
49c	**c,** d, i, r, **t** (URI)	c, i, r, t (URI)
59	c, i, t	—
62a	c, i, r	—
63	d, r, t	—
2a	—	t, **f**
7b	—	c
24b	FVC, –14.6% FEF_{max}, –20%	—
64b	—	FVC, –8.0% FEV_1, –9.1%
Divers 3a, 13b, 21, 29, 57 No symptoms or signs		

Roman font indicates mild, and bold indicates moderate symptoms. Abbreviations: “c” is cough, “d” is dyspnea (shortness of breath), “i” is inspiratory burning, “r” is rapid shallow breathing, and “t” is chest pain or tightness. “URI” is upper respiratory infection; “f” is fatigue or exercise intolerance. Diver numbers represent individuals numbered in the sequence enrolled, and “a”, “b”, etc., represent repeated dives by the same subject.

Profile A2

Table 2.
Decreases in pulmonary function and symptoms of pulmonary oxygen toxicity after Profile A2

Diver	During or immediately after dive	Day+1	Day+2
2b	c, t, **f**	—	
7a	c	—	
11b	i FEV_1, –14.7% $FEF_{25–75}$, –40%	f FEV_1, –17.0% $FEF_{25–75}$, –42%	FEV_1, –13.4% $FEF_{25–75}$, –37%
17	**i**, c	c	
48	c		
53b	d, t FVC, –10.1% FEV_1, –9.8%	—	
34b		c, f (URI)	
58a	t	—	
33b	i*	$FEF_{25–75}$, –21%	
6b	FEF_{max}, –17%		
8a	—	$FEF_{25–75}$, –17%	
8b	—	$FEF_{25–75}$, –19%	
32b	—	$FEF_{25–75}$, –21%	
52b	FVC, –9.4%	—	
54a	FVC, –13.9% FEV_1, –11.8%	—	
19	Probable ingestion or aspiration of water contaminated with CO_2 absorbent, “caustic cocktail.”		
	t, *r*, ***i, c*** FVC, –13.0% FEV_1, –22.4% FEF_{max}, –32% $FEF_{25–75}$, –29%	t, **r**, i, c, ***f*** FVC, –11.4% FEV_1, –11.3%	c, f
Divers 3b, 5b, 12b, 15a, 25, 28b, 42, 52a, 56, 62 No symptoms or signs			

Roman font indicates mild; bold, moderate; italic, moderately severe; and bold italic, severe symptoms. Abbreviations: “c” is cough, “d” is dyspnea (shortness of breath), “f” is fatigue or exercise intolerance, “i” is inspiratory burning, “i*” is throat irritation, “r” is rapid shallow breathing, and “t” is chest pain or tightness. “URI” is upper respiratory infection. Diver numbers represent individuals numbered in the sequence enrolled, and “a”, “b”, etc., represent repeated dives by the same subject.

Nine of 26 subjects reported respiratory symptoms during the dive or immediately after surfacing, but one of them most likely suffered from a “caustic cocktail” — that is, ingestion or aspiration of water contaminated with caustic CO_2 absorbent. Although his symptoms and changes in pulmonary function are indicated in Table 2, they are not included in the statistics reported here.

On the day of diving, eight of 25 subjects reported respiratory symptoms unrelated to caustic cocktail. For one, symptoms continued for another day. One subject reported symptoms only on the first day after diving, but in conjunction with other symptoms of a URI that probably explained his cough; he is not included in the incidence numbers.

Five divers showed decreases in pulmonary function after the dive, and for one, the deficits lasted more than two days. Four subjects had decreased flow-volume parameters only on Day+1. On dive day, two of the subjects both reported symptoms and showed decreases in indices of pulmonary function.

After Profile A2 (60 minutes of exercise; 6 hours and 33 minutes of oxygen time), the incidence of symptoms on the dive day was 32.0%, with binomial CI 14.9% to 53.5%, and on Day+1 it was one of 19 (5.3%), with binomial CI 0.1% to 26.0%. The incidence of changes in pulmonary function after the dive was 20.0%, with binomial CI 6.8% to 40.7%, and on Day+1, it was five of 19 subjects (26.3%), binomial CI 5.1% to 51.2%. Two of 19 subjects reported fatigue or exercise intolerance on Day+1.

Profile A3

Eight of 22 subjects reported respiratory symptoms during the dive or immediately after surfacing, but only one of 17 reported such symptoms on Day+1. Six of 20 subjects showed decreased flow-volume parameters on the dive day, as did three on Day+1.

In calculating the incidences of symptoms for this profile, we included Diver 25c on both the dive day and Day+1, despite his URI symptoms on Day+1. His similar symptoms on both days, in conjunction with mild but measurable decreases in FVC and FEV_1 immediately postdive, suggest that at least some of his symptoms had a dive-related cause.

For Subject 60, pulmonary function remained depressed until Day+6, although it was beginning to improve. His injury may have been so persistent because he had continued with exercise as heavy as he could tolerate, an exercise level that he reported was much lower than usual. The subject was lost to follow-up because he travelled.

After Profile A3 (49 minutes of exercise; 6 hours and 42 minutes of oxygen time), the incidence of symptoms on the dive day was 36.4%, with binomial CI 17.2% to 59.4%, and on Day+1 it was 6%, with binomial CI 0.1% to 28.7%. The incidence of changes in pulmonary function after the dive was 27.3%, with binomial CI 10.7% to 50.2%, and on Day+1 it was 17.6%, with binomial CI 3.8% to 43.4%. Three subjects reported exercise intolerance, two after diving, and one for multiple days postdive.

Table 3.
Decreases in pulmonary function and symptoms of pulmonary oxygen toxicity after Profile A3

Diver	**During or immediately after dive**	**Day+1**	**Day+2**
22a	**c**, *d*, i, r, **t, f** FVC, –17.2% FEV_1, –19.3% $FEF_{25–75}$, –25%	—	—
22b	**d**, **i**, **f**		
22c	**c**, **d**, **i**, t		
25c	c, d, t FVC, –10.5% FEV_1, –12.0%	c, d, t (URI)	
27a	i		
28a	i, t		
60	c FEV_1, –10.0%	f FEV_1, –9.9% $FEF_{25–75}$, –22%	**f** FEV_1, –12.0% $FEF_{25–75}$, –33%
66	c		
6a	FEF_{max}, –20%	FEF_{max}, –22%	
15b	$FEF_{25–75}$, –25%	$FEF_{25–75}$, –27%	
65	FVC, –8.4% FEV_1, –9.4%		
Divers 1, 2c, 5a, 16, 24, 25b, 30, 41, 43, 45, 47 No symptoms or signs			

Roman font indicates mild; bold, moderate; and italic, moderately severe symptoms.
Abbreviations: “c” is cough, “d” is dyspnea (shortness of breath), “f” is fatigue or exercise intolerance, “i” is inspiratory burning, “r” is rapid shallow breathing, and “t” is chest pain or tightness. “URI” is upper respiratory infection.
Diver numbers represent individuals numbered in the sequence enrolled, and “a”, “b”, etc., represent repeated dives by the same subject.

Profile A4

Five of 25 subjects reported symptoms on the dive days of Profile A4, but two reports were from the same subject, who reported only cough in conjunction with a URI — symptoms not considered to be effects of the dive. On Day+1 the subject with a URI was the only one of 22 subjects to report respiratory symptoms, and only his chest tightness on Day+1 seems more likely to result from pulmonary oxygen toxicity than from the infection. Three subjects, one with symptoms and two without, showed decreases in flow-volume parameters on the day of diving. Three other subjects had flow-volume decreases on Day+1.

Table 4.
Decreases in pulmonary function and symptoms of pulmonary oxygen toxicity after Profile A4

Diver	**During or immediately after dive**	**Day+1**	**Day+2**
27b	i		
49a	c (URI)	**c** (URI)	
49b	c (URI)	c, t (URI)	
53a	t FVC, –8.5% FEV_1, –9.6% FEF_{max}, –20%		
58b	c, t	FVC, –8.1% FEV_1, –10.5%	f FVC, –7.7% FEV_1, –9.5%
12a	FEF_{max}, –26%		
15c	$FEF_{25–75}$, –22%		
32a		$FEF_{25–75}$, –21%	
64a		f FVC, –8.8%	
Divers 9a,b,c, 10a,b, 12b, 13a, 20, 26a,b 33a, 34a, 37, 38, 39, 40 No symptoms or signs			

Roman font indicates mild, and bold indicates moderate symptoms. Abbreviations: “c” is cough, “d” is dyspnea (shortness of breath), “f” is fatigue or exercise intolerance, “i” is inspiratory burning, “r” is rapid shallow breathing, and “t” is chest pain or tightness. “URI” is upper respiratory infection.
Diver numbers represent individuals numbered in the sequence enrolled, and “a”, “b”, etc., represent repeated dives by the same subject.

After Profile A4 (56 minutes of exercise; 6 hours and 56 minutes of oxygen time), the incidence of symptoms related to pulmonary oxygen toxicity immediately after diving is three of 25 subjects (12%), with binomial CI of 2.5% to 31.3%, while that on Day+1 is one of 22 (4.5%), with binomial CI of 0.1% to 22.9%. The incidence of depressed flow-volume parameters on the day of diving is 12%, with binomial CI of 2.5% to 31.3%, and that on Day+1 is 13.6% with binomial CI of 2.9% to 35%.

Two subjects reported low exercise tolerance, both in conjunction with mild flow-volume changes. For one of them, subject 58b, deficits in FVC and FEV_1 similar to those on Day+1 persisted for at least four days, until the subject was lost to follow-up.

SUMMARY AND SEVERITY OF INCIDENTS

The incidences and their 95% confidence intervals are shown by profile in Figures 1–2.

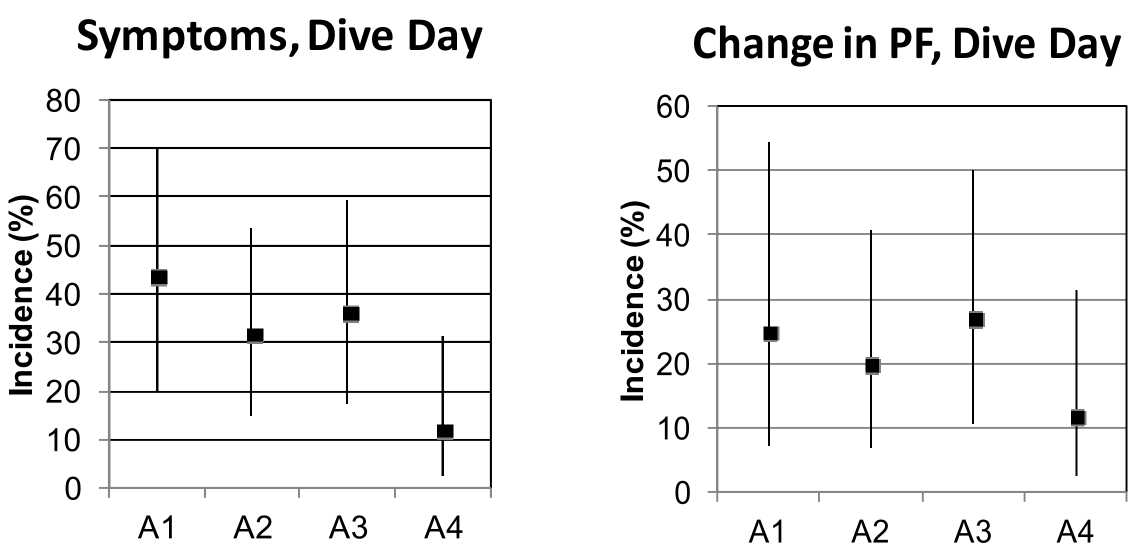

Figure 1. Incidences of symptoms and changes in pulmonary function (PF), dive days. The numbers of subjects with at least one symptom or flow-volume change, divided by the total numbers of subjects, are shown for each dive profile, with binomial 95% confidence intervals.

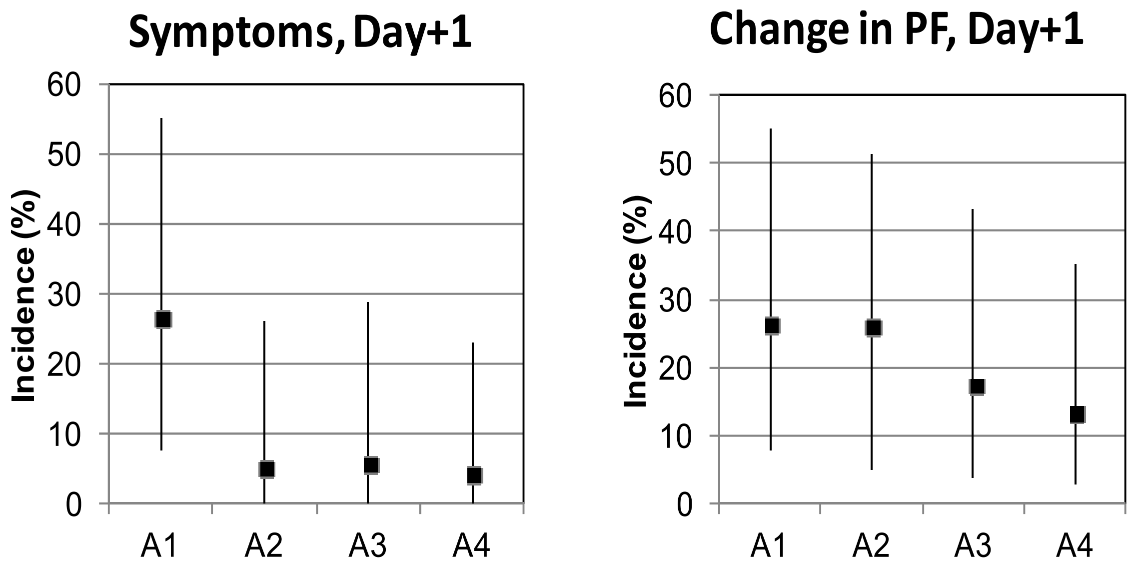

Figure 2. Incidences of symptoms and changes in pulmonary function (PF), Day+1s. The numbers of subjects with at least one symptom or flow-volume change, divided by the total numbers of subjects, are shown for each dive profile, with binomial 95% confidence intervals.

Although the binomial 95% confidence intervals overlap for all profiles, Fisher's Exact Test[5] indicates that the incidence of symptoms on the Profile A1 dive days (44%) was significantly higher ($p<0.04$) than that on the Profile A4 dive days (12%) (Fig.1), but that the difference (A1: 27%, A4: 5%) was not significant at the 90% confidence level on Day+1 ($p>0.13$) (Fig. 2). With 90% but not with 95% confidence in the estimate, the incidence of symptoms on dive days also was higher ($p<0.09$) with Profile A3 (36%) than with Profile A4 (Fig. 1). Incidences of symptoms did not differ pairwise for other profiles, and incidences of changes in pulmonary function parameters did not differ across profiles.

Symptoms were most severe after Profile A3, when two subjects reported four or more concurrent symptoms, with several of them moderate and one moderately severe. The greatest magnitude of changes in FVC and FEV_1 also occurred with this profile (Table 5). After Profile A2, most symptoms were mild, although one subject reported moderate inspiratory burning and three subjects reported having two symptoms concurrently. This was the profile with the most severe change in $FEF_{25–75}$ (Table 5). After Profile A1, most symptoms were mild: the one moderate symptom appeared with a URI, but four subjects reported three or more concurrent symptoms, and the greatest change in $FEF_{25–75}$ was similar to that for Profile A2 (Table 5). However, after Profile A4, no subject reported more than one symptom: the only symptom greater than mild was ascribed to a URI, and the greatest changes in all but FEF_{max} were considerably less than those for the other profiles (Table 5).

On dive days for all profiles combined, 25% of subjects reported respiratory symptoms and 19% showed decreases in one or more flow-volume index. On Day+1, 9.6% of divers reported respiratory symptoms, 19% had flow-volume deficits, and 9% mentioned exercise intolerance.

Table 5.
Most severe changes in pulmonary function after each profile, dive day or Day+1

Profile	FVC	FEV_1	FEF_{max}	$FEF_{25–75}$
A1	–14.6%	–18.2%	–20%	–40%
A2	–10.1%	–17.0%	–17%	–42%
A3	–17.2%	–19.3%	–22%	–27%
A4	–8.8%	–10.5%	–26%	–22%

As listed in Table 6, some pulmonary function variables changed overall after these dives. FVC and FEV_1 decreased on the average on dive day of Profile A1, as did FEV_1 on Day+1 after Profiles A3 and A4. Average $FEF_{25–75}$ decreased on Day+1 after Profiles A1 and A3. However, FEF_{max} was greater than baseline on Day+1 for Profile A1 and on dive day and Day+1 for Profile A4.

Table 6.
Significant mean changes in pulmonary function variables on dive day (D) or Day+1 (D+1)

	FVC			FEV_1			FEF_{max}			$FEF_{25–75}$		
	mean	SE	p<	mean	SE	p<	mean	SE	p<	mean	SE	p<
A1: D	–2.5%	0.011	0.04	–3.5%	0.013	0.02						
D+1							9.6%	0.042	0.05	–10.1	0.035	0.02
A2: D												
D+1												
A3: D							–0.7%	0.019	0.02			
D+1				–2.4%	0.008	0.01				–5.3%	0.022	0.03
A4: D							5.7%	0.027	0.05			
D+1				–2.0%	0.009	0.04	9.4%	0.034	0.02			

Significant **increases** are shaded.

Despite the few average decreases (Table 6), the frequency distributions (Figs. 3–6) show that changes in most pulmonary function variables were isolated events rather than trends for the entire population. For the most part, the distributions are centered near zero change, but with some skewing toward decreased values and with some apparent outliers that represent real events in a few people. For FEF_{max}, however, the frequency distributions show a systematic shift to values greater than those of baseline on dive days and later.

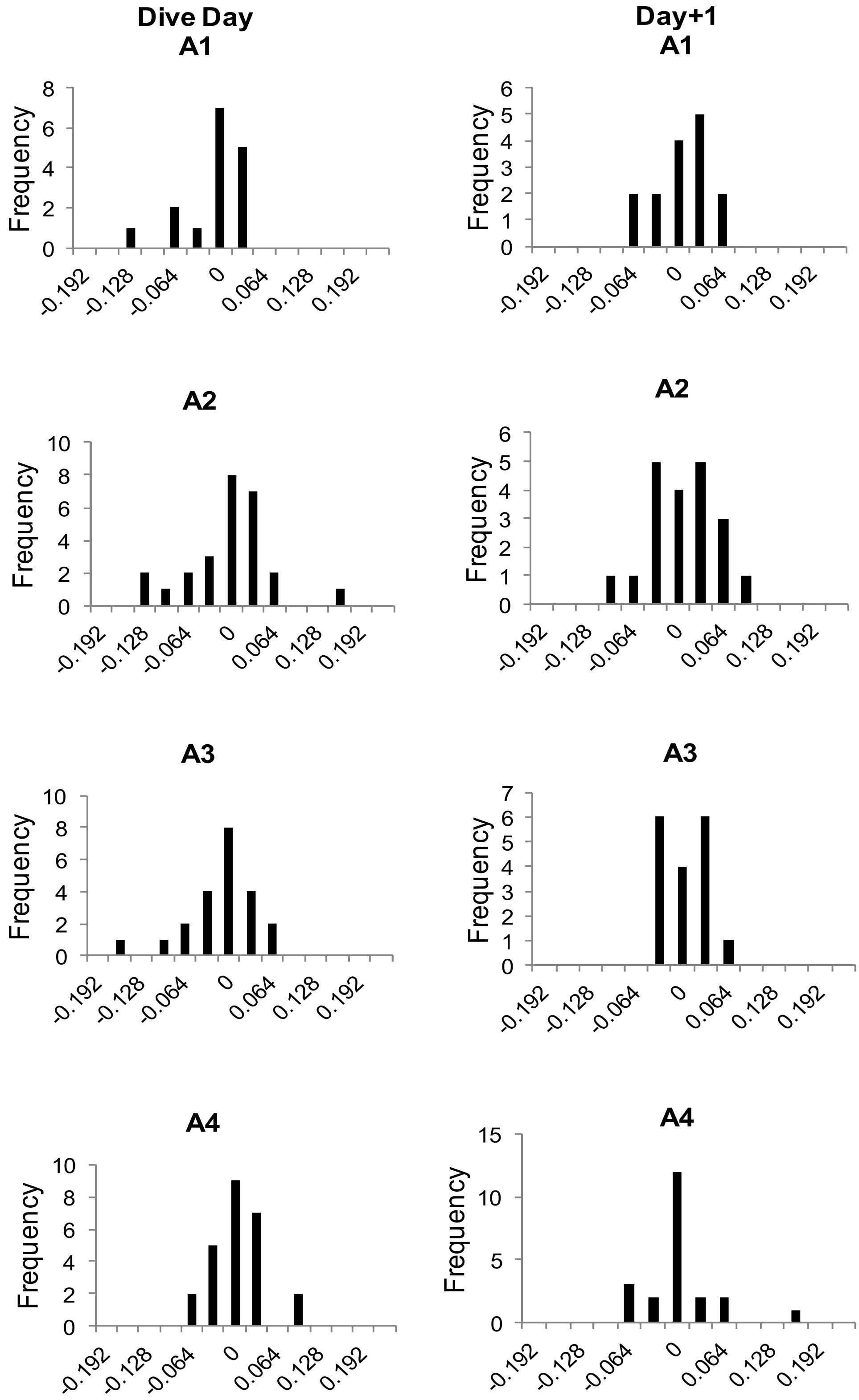

Figure 3. Distribution of relative changes in FVC, individual dive profiles. Bin size is one coefficient of variation (CV) for normal variability in the dry.[3]

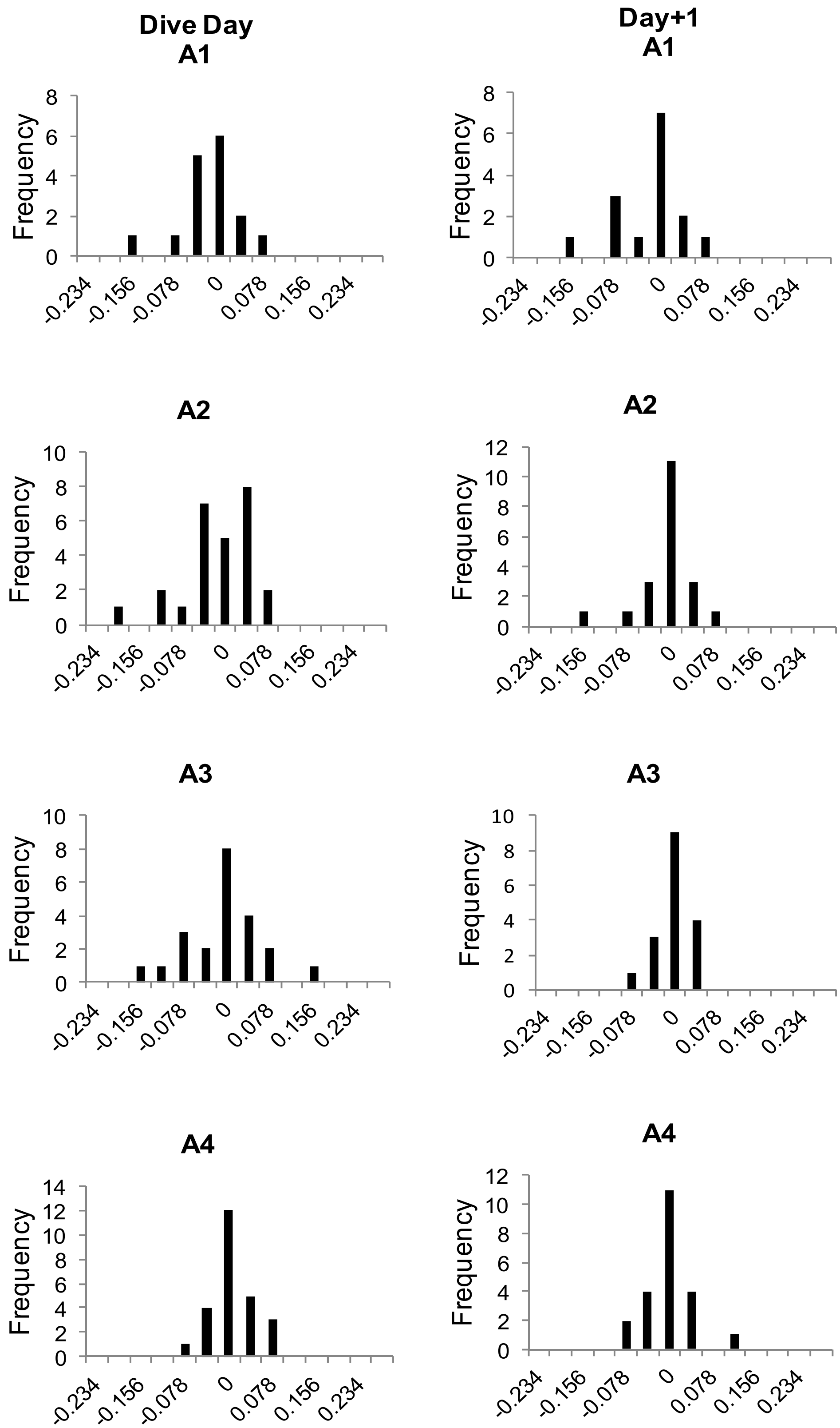

Figure 4. Distribution of relative changes in FEV_1, individual dive profiles. Bin size is one CV for normal variability in the dry.[3]

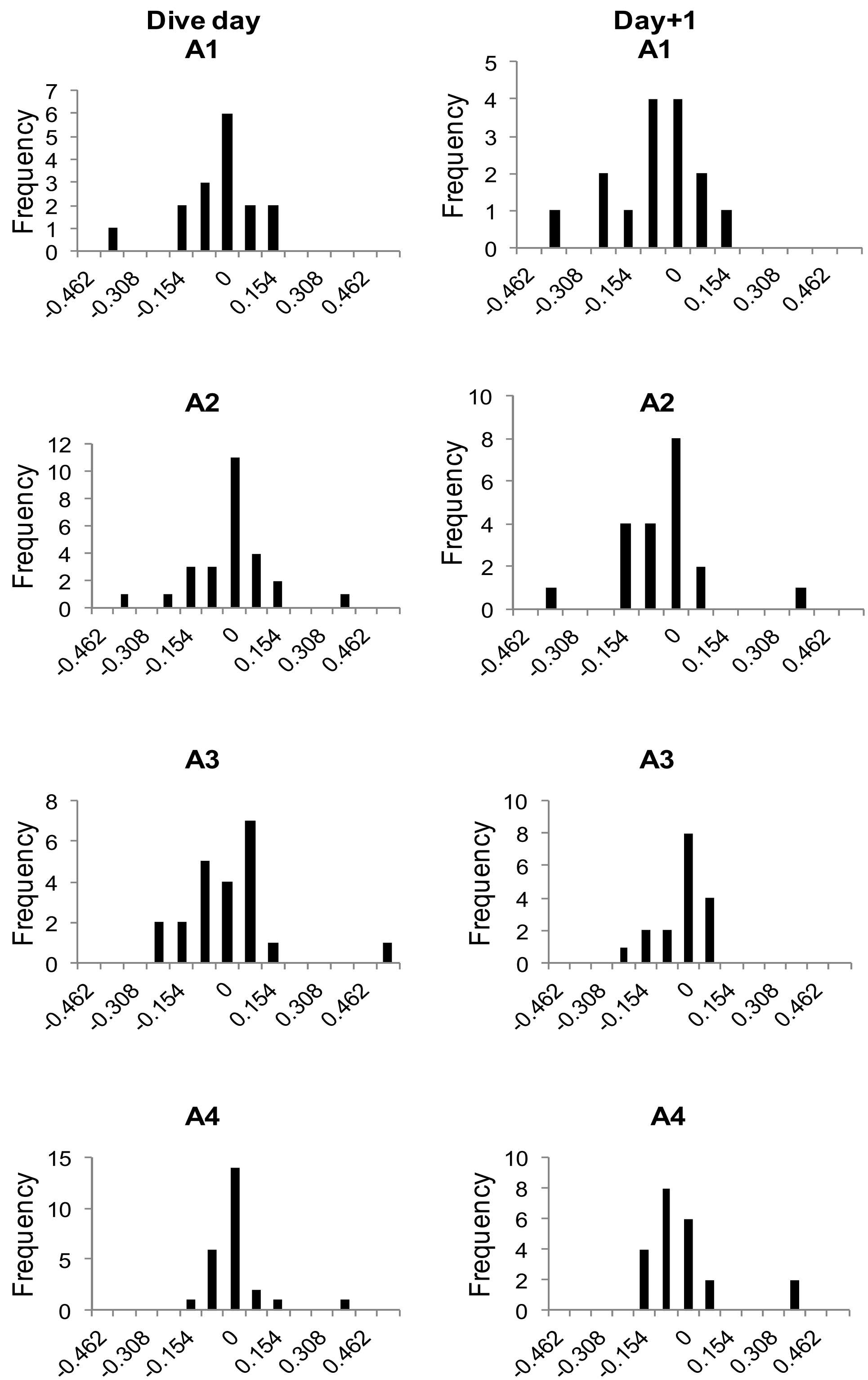

Figure 5. Distribution of relative changes in mid forced expired flow ($FEF_{25–75}$), individual dive profiles. Bin size is one CV for normal variability in the dry.[3]

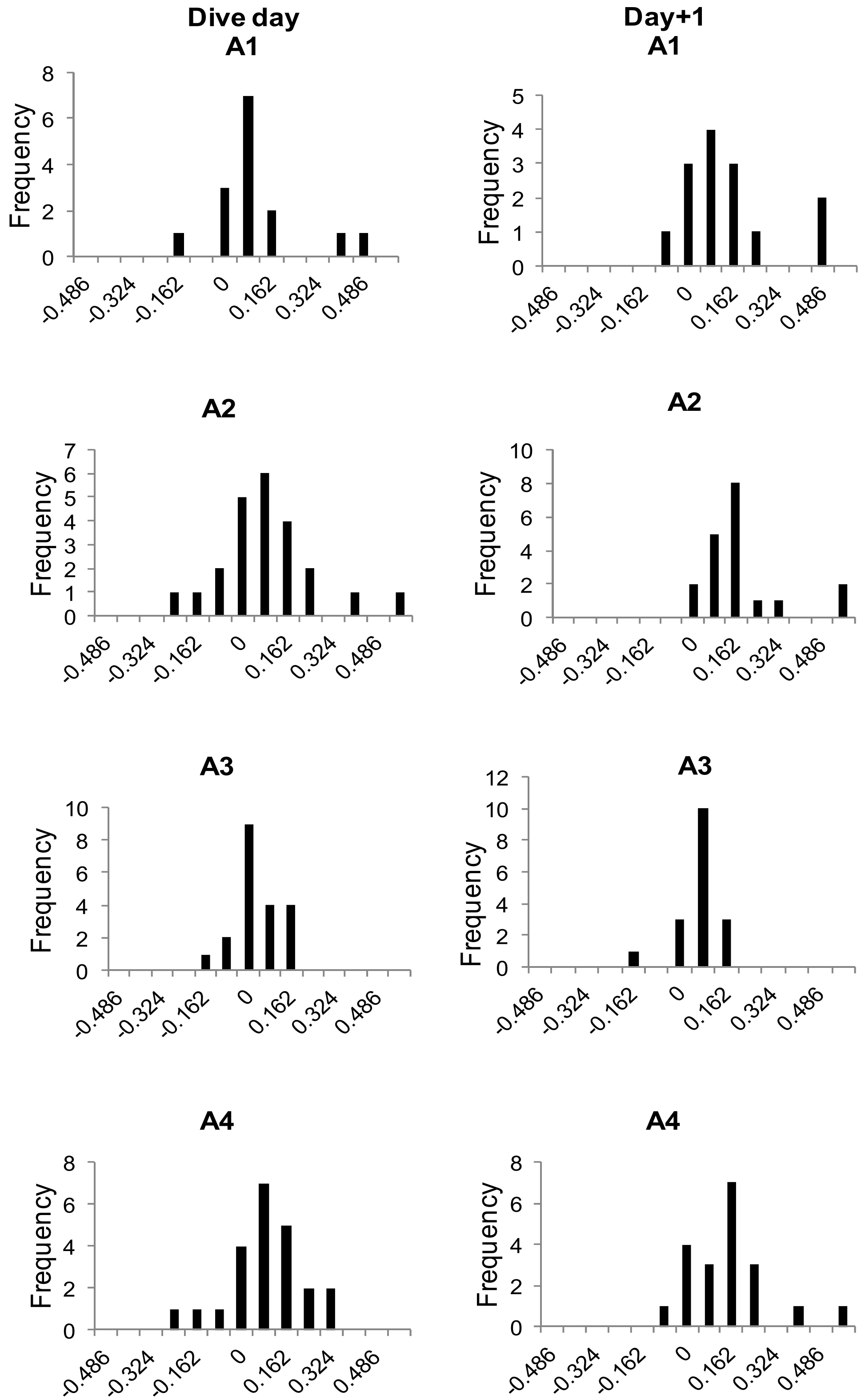

Figure 6. Distribution of relative changes in peak flow (FEF_{max}), individual dive profiles. Bin size is one CV for normal variability in the dry.[3]

DISCUSSION

In previous work we found that pulmonary effects after eight-hour dives with PO_2 = 1.3 atm were similar at three dive depths (three different inspired oxygen fractions) and with various breathing gear: at 50 feet, when divers used the MK 16 MOD 1 with nitrogen as the inert gas; at about 12 feet of fresh water, when divers breathed surface-supplied O_2 from the MK 20 mask,[6] and at 20 fsw, when divers breathed surface-supplied, mixed N_2 and O_2 from the MK 20 mask.[7] In the eight-hour, 50-foot MK 16 dives and the eight-hour shallow, 100% O_2 dives, 41% and 43% of subjects, respectively, had respiratory symptoms on surfacing, when 29% and 13% respectively showed decreases in pulmonary function.[6] Profiles A1–A3 of the current series (approximately seven-hour exposures) had incidences of symptoms and decreases in pulmonary function (Figs. 1 and 2) similar to those of the previous eight-hour dives. No difference in pulmonary effect seems evident between the N_2 and He background gases, just as the fraction of inert gas (or oxygen) or the breathing apparatus seems to be unimportant at constant PO_2.

Our subjects were all highly motivated to perform the pulmonary function testing well, but many were inexperienced. The variable most sensitive to effort, FEF_{max}, generally increased from baseline to later measurements (Fig. 6) as the subjects learned how to perform the maneuver better. Even baseline measurements were internally reproducible, though, indicating clean measurements of the effort-independent portions of the flow-volume curve. Conveniently, any decrease in FEF_{max} after diving exposure to O_2, a decrease that would be masked by the learning effect, is most likely to represent airway irritation and burning which should have been noted as symptoms. Any changes in FEV_1 caused by increased peak flow with experience would reduce any measured decreases, but probably within the error bounds of the measurement.

We attribute the increase of FEF_{max} with time to increased subject experience, not to the diving exposures. Expiratory flow is always the ratio of driving pressure to effective airway resistance, and thus can increase if either driving pressure increases or resistance decreases. For FEF_{max}, the driving pressure is the sum of recoil pressure of lung and chest wall at almost total lung capacity (TLC), plus the intrapleural pressure generated voluntarily by the subject initiating the maneuver. The primary airway resistance is in the bronchi because total airway cross section there is lowest and all airways are held open by distended lung tissue. No mechanism of oxygen exposure or of diving is likely to have distended the bronchi. Driving pressure could have increased because, implausibly, diving made the lung tissue stiffer, but only at TLC (other measures did not change), or because subjects contracted their expiratory muscles harder or faster with increased practice; because recoil pressure drops very quickly with decrease in lung volume, peak flow is very sensitive to the rate at which the subject increases pressure in his or her chest. We are left with the very plausible explanation that FEF_{max} increased after diving because more practiced subjects either generated higher expiratory pressures at the start of forced vital capacity maneuvers or generated the expiratory pressures faster.

The largest changes in flow-volume parameters, when they occurred, were in the effort-independent $FEF_{25–75}$, and the most commonly measured change was in FEV_1. Both of these measures suggest that oxygen exposure sometimes generated interstitial edema, but more often increased the resistance of small airways.

$FEF_{25–75}$ depends largely on the static recoil of the lung and on the resistance of the small airways,[8] while FEV_1 is influenced by lung recoil and both large and small airway resistance. Lung static recoil could be reduced after oxygen exposure by the development of interstitial edema, that is, accumulation of liquid within lung membranes. Unfortunately, because we did not measure diffusing capacity of the lung, we do not have an independent measure to confirm or exclude its presence; the changes in vital capacity caused by membrane swelling are within the error of the measurement. Interstitial edema seems unlikely to occur without respiratory symptoms and reduced exercise tolerance, but may have been present in symptomatic subjects with large changes in $FEF_{25–75}$ and FEV_1, for example, Subject 11 after Profiles A1 and A2, and subject 60 after Profile A3.

Most of the decreases in $FEF_{25–75}$ and FEV_1 are probably ascribable to increased resistance of small airways. Small airway resistance will increase if airway diameter is reduced, for example by fluid cuffing, that is, liquid accumulation in the tissue spaces around the airways and their branch points. Increased mucous production in response to irritation also can decrease effective airway diameter in airways as small as the terminal bronchioles. Changes in FVC most likely also resulted from small airway closure at low lung volume because of fluid cuffing and increased mucous production.

The exposures of Profile A4 appear to have been milder than those of Profile A1, which had similar incidences of symptoms and changes in pulmonary function similar to those reported in the past.[6,7] On dive days Profiles A2 and A3 were similar to Profile A1, and on Day+1, to A4. We seek an explanation for the difference between Profile A4 and profile A1 and other seven- to eight-hour exposures to PO_2 = 1.3.

A comparison of the dive profiles from A1 to A4 yields few differences.

1. Profile A4, with maximum depth of 160 fsw, was the shallowest of the HeO_2 profiles, as compared to that of 200 fsw for Profile A1.

2. The total time with PO_2 = 1.3 atm — that is, the sum of the times breathing from the MK 16 MOD 1 with PO_2 = 1.3 atm and from the MK 25 at 20 fsw — was identical for Profiles A1 and A4: 6 hours and 56 minutes. For Profile A3, time at elevated PO_2 was 6 hours and 42 minutes, and for Profile A2, it was 6 hours and 33 minutes.

3. All profiles included 45 minutes of air breathing at 20 fsw.

4. The maximum difference in time on the MK 25 was 5 minutes.

5. In Profiles A1 and A4, time in the water differed by only 2 minutes (A1, 3 hours and 19 minutes; A4, 3 hours and 21 minutes). Profile A3 included 3 hours and 15 minutes in the water, and Profile A2, 2 hours and 27 minutes.

6. Profile lengths of stay at maximum depth, from the longest to the shortest times, were the following: for A2, 64 minutes at 200 fsw; for A1, 47 minutes at 200 fsw; for A4, 59 minutes at 160 fsw; and for A3, 53 minutes at 180 fsw. The order here makes time at depth an unlikely cause of the difference between A4 and all the other profiles.

7. Profiles ranked by exercise time, from the longest to the shortest, are the following: for A2, 60 min; for A4, 56 min; for A3, 49 min; and for A1, 43 min. Duration of exercise is thus another unlikely variable. Further, although exercise appears to slow recovery from pulmonary oxygen toxicity,[9] these single dives with one hour or less of exercise would not be expected to differ in pulmonary effects from those without exercise — and thus, not to differ among themselves.

The most obvious difference within this HeO_2 dive series is that of the maximum depth for Profiles A1 and A4, which could have affected P_{O_2} overshoots or external and internal work of breathing. Overshoots might have made A1 a more severe exposure than A4, but they cannot explain the differences in incidences of symptoms or changes in pulmonary function between Profile A4 and the previously reported N_2O_2[6,7] or O_2 dives.[7]

The external work of breathing the MK 16 MOD 1 with HeO_2 is only 5% to 6% less at 165 fsw than it is at 198 fsw.[10] Internal work of breathing also is less at 165 fsw than at 200 fsw; the pressure to overcome internal airway resistance increases approximately linearly with increasing gas density (ρ).[11]

Table 7 lists ρ relative to surface air and to the most shallow dives among all available seven- and eight-hour dives with P_{O_2} = 1.3 atm. Clearly, differences in ρ cannot explain the different severities of the profiles. In Table 7, the profiles of this and previous studies are arranged in order of gas density, from the lowest to the highest. At depth, the gas density for Profile A4 was only about 8% less than that for Profile A1. Furthermore, gas density in Profile A4 was intermediate between that of the previously reported N_2O_2[6, 7] or O_2 dives,[7] yet the pulmonary effects of those studies had been very similar to one another.

Depending on the flow regime, pressure to drive flow is a function of ρ, viscosity (μ), or a combination of the two. At moderately high airflow, the resistive pressure drop across the airways can be expected to be proportional to $\rho^{1.5}\ \mu^{0.5}$.[12] However, the differences in μ across the gases of interest are small — 18, 19, and 20 μPa · s for N_2, He, and O_2, respectively — and our studies' order of ranking by $\rho^{1.5}\ \mu^{0.5}$ is the same as that by ρ alone (Table 5).

Table 7.
Relative density (ρ) and viscosity (μ) effects — pulmonary oxygen toxicity studies with PO_2 = 1.3 atm

Profile	Gas	Depth (fsw)	Total pressure (atm)	O_2 fraction	ρ normalized by surface air	ρ normalized by O_2 at 12 fsw	$\rho^{1.5}\ \mu^{0.5}$ normalized to O_2 at 12 fsw
Shykoff[7]	O_2	12	1.36	1.00	1.50	1.00	1.00
Shykoff[7]	N_2O_2	20	1.61	0.81	1.73	1.15	1.17
A4	HeO_2	160	5.85	0.22	2.06	1.37	1.56
A3	HeO_2	180	6.45	0.20	2.15	1.43	1.66
A1, A2	HeO_2	200	7.06	0.18	2.23	1.48	1.76
Shykoff[6]	N_2O_2	50	2.52	0.52	2.61	1.73	2.16

The different outcomes of Profile A4 and those of the other profiles are unexplained by differences in the profiles themselves. Differences among divers, particularly in their levels of experience with experimental diving or with pulmonary function testing, are another possible explanation: young or inexperienced divers are likely to underreport symptoms. Several divers mentioned long after the study that they had indeed had symptoms that they denied. Measurements of differences in pulmonary function can be compromised by poor baseline measurements resulting from lack of practice with flow-volume maneuvers. However, those differences should have been evenly distributed across profiles. The profiles were intermingled across the three months of testing (i.e., divers from all commands involved in testing participated in all the profiles), and some divers dove in more than one profile. Figure 6 suggests that inexperience at baseline testing, inexperience evident as increased FEF_{max} as testing progressed, was distributed across all profiles. Reasons for Profile A4 to differ from the others remain elusive.

CONCLUSIONS

The results from Profiles A1–A3 with HeO_2 (PO_2 = 1.3 atm) at depth, followed by chamber air, and then with O_2 from the MK 25, show incidences and severity of pulmonary oxygen toxicity consistent with earlier studies. Here, 30% to 40% of subjects experienced symptoms, usually mild, on the day of diving Profiles A1 – A3, and just over 10% reported symptoms on the day of diving Profile A4, and 20% to 30% showed mild deficits in pulmonary function immediately after diving. Although many divers will have no pulmonary problems after these exposures, some will. And that pulmonary toxicity, if or when it occurs, could compromise a mission.

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